



endo sequence from Collagen XVIII.

Sequence Range: 1-555

Nucleotide 1 = Start for Endostatin and fragments EM1 and EM2.

EM1 fragment ends at nucleotide 525, EM2 fragment ends at nucleotide 501.

5	10	15	20	25	30	35	40	45							
CAT	ACT	CAT	CAG	GAC	TTT	CAG	CCA	GTG	CTC	CAC	CTG	GTG	GCA	CTG	AAC
GTA	TGA	GTA	GTC	CTG	AAA	GTC	GGT	CAC	GAG	GTG	GAC	CAC	CGT	GAC	TTG
50	55	60	65	70	75	80	85	90	95						
ACC	CCC	CTG	TCT	GGA	GGC	ATG	CGT	GGT	ATC	CGT	GGA	GCA	GAT	TTC	CAG
TGG	GGG	GAC	AGA	CCT	CCG	TAC	GCA	CCA	TAG	GCA	CCT	CGT	CTA	AAG	GTC
100	105	110	115	120	125	130	135	140							
TGC	TTC	CAG	CAA	GCC	CGA	GCC	GTG	GGG	CTG	TCG	GGC	ACC	TTC	CGG	GCT
ACG	AAG	GTC	GTT	CGG	GCT	CGG	CAC	CCC	GAC	AGC	CCG	TGG	AAG	GCC	CGA
145	150	155	160	165	170	175	180	185	190						
TTC	CTG	TCC	TCT	AGG	CTG	CAG	GAT	CTC	TAT	AGC	ATC	GTG	CGC	CGT	GCT
AAG	GAC	AGG	AGA	TCC	GAC	GTC	CTA	GAG	ATA	TCG	TAG	CAC	GCG	GCA	CGA
195	200	205	210	215	220	225	230	235	240						
GAC	CGG	GGG	TCT	GTG	CCC	ATC	GTC	AAC	CTG	AAG	GAC	GAG	GTG	CTA	TCT
CTG	GCC	CCC	AGA	CAC	GGG	TAG	CAG	TTG	GAC	TTC	CTG	CTC	CAC	GAT	AGA
245	250	255	260	265	270	275	280	285							
CCC	AGC	TGG	GAC	TCC	CTG	TTT	TCT	GGC	TCC	CAG	GGT	CAA	CTG	CAA	CCC
GGG	TCG	ACC	CTG	AGG	GAC	AAA	AGA	CCG	AGG	GTC	CCA	GTT	GAC	GTT	GGG
290	295	300	305	310	315	320	325	330	335						
GGG	GCC	CGC	ATC	TTT	TCT	TTT	GAC	GGC	AGA	GAT	GTC	CTG	AGA	CAC	CCA
CCC	CGG	GCG	TAG	AAA	AGA	AAA	CTG	CCG	TCT	CTA	CAG	GAC	TCT	GTG	GGT
340	345	350	355	360	365	370	375	380							
GCC	TGG	CCG	CAG	AAG	AGC	GTA	TGG	CAC	GGC	TCG	GAC	CCC	AGT	GGG	CGG
CGG	ACC	GGC	GTC	TTC	TCG	CAT	ACC	GTG	CCG	AGC	CTG	GGG	TCA	CCC	GCC
385	390	395	400	405	410	415	420	425	430						
AGG	CTG	ATG	GAG	AGT	TAC	TGT	GAG	ACA	TGG	CGA	ACT	GAA	ACT	ACT	GGG
TCC	GAC	TAC	CTC	TCA	ATG	ACA	CTC	TGT	ACC	GCT	TGA	CTT	TGA	TGA	CCC
435	440	445	450	455	460	465	470	475	480						
GCT	ACA	GGT	CAG	GCC	TCC	TCC	CTG	CTG	TCA	GGC	AGG	CTC	CTG	GAA	CAG
CGA	TGT	CCA	GTC	CGG	AGG	AGG	GAC	GAC	AGT	CCG	TCC	GAG	GAC	CTT	GTC
485	490	495	500	505	510	515	520	525							
AAA	GCT	GCG	AGC	TGC	CAC	AAC	AGC	TAC	ATC	GTC	CTG	TGC	ATT	GAG	AAT
TTT	CGA	CGC	TCG	ACG	GTG	TTG	TCG	ATG	TAG	CAG	GAC	ACG	TAA	CTC	TTA
530	535	540	545	550	555										
AGC	TTC	ATG	ACC	TCT	TTC	TCC	AAA	TAG							
TCG	AAG	TAC	TGG	AGA	AAG	AGG	TTT	ATC							

Fig. 1

BEST AVAILABLE COPY

Sequence Range: 1 to 184

5	10	15	20	25	30	35	40	45						
HTH	QDF	QPV	LHL	VAL	NTP	LSG	GMR	GIR	GAD	FQC	FQQ	ARA	VGL	SGT
50	55	60	65	70	75	80	85	90						
FRA	FLS	SRL	QDL	YSI	VRR	ADR	GSV	PIV	NLK	DEV	LSP	SWD	SLF	SGS
95	100	105	110	115	120	125	130	135						
QGQ	LQP	GAR	IFS	FDG	RDV	LRH	PAW	PQK	SVW	HGS	DPS	GRR	LME	SYC
140	145	150	155	160	165	170	175	180						
ETW	RTE	TTG	ATG	QAS	SLL	SGR	LLE	QKA	ASC	HNS	YIV	LCI	ENS	FMT
SFS	K													

Fig. 2

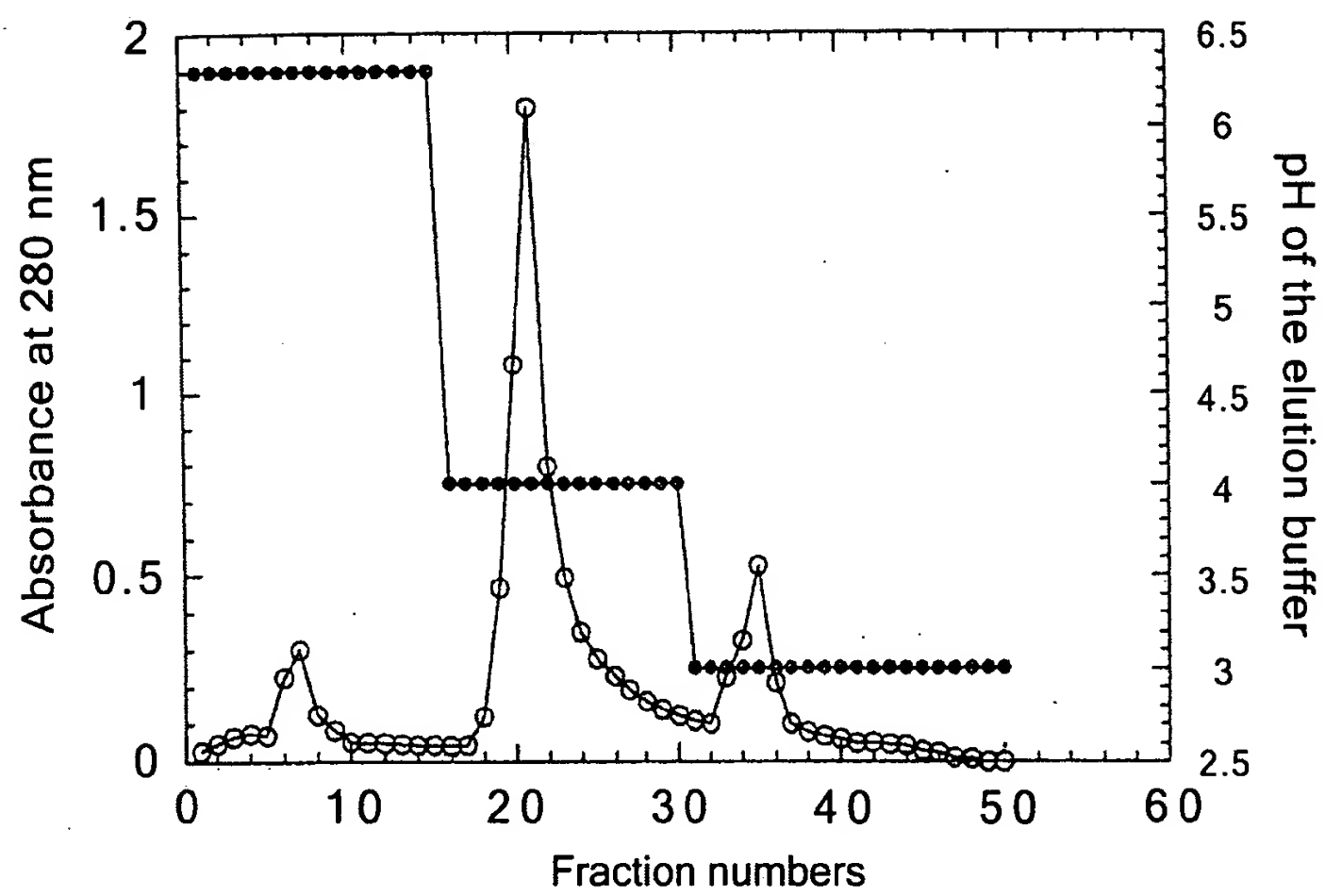


Fig. 3

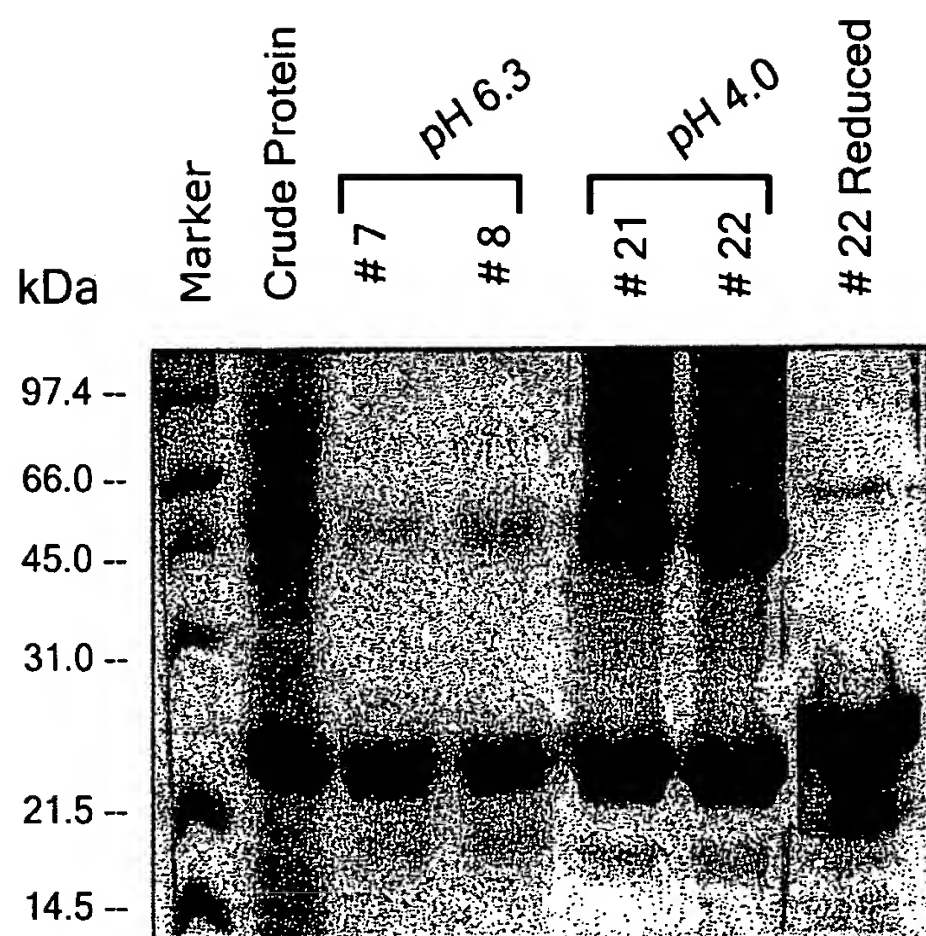


Fig. 4

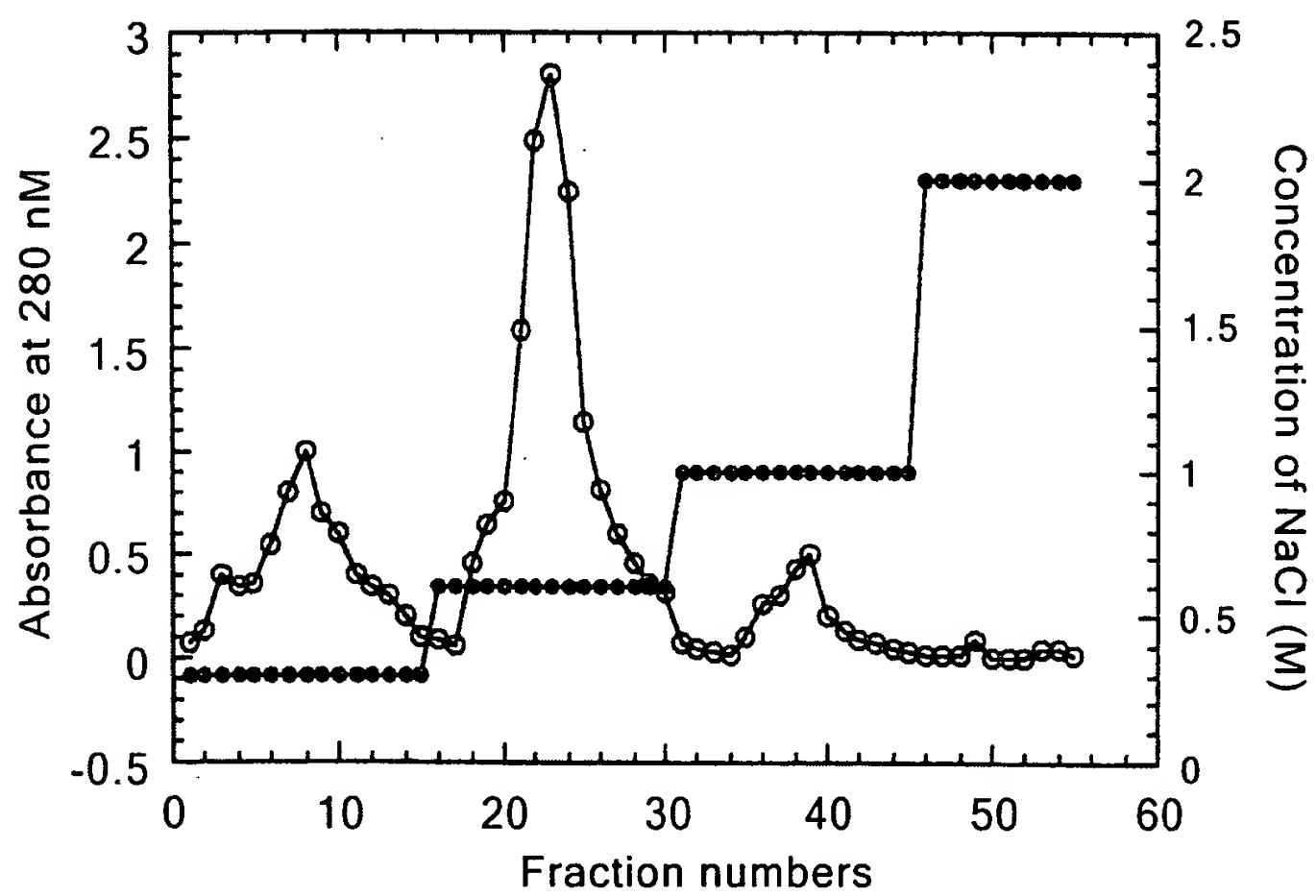


Fig. 5

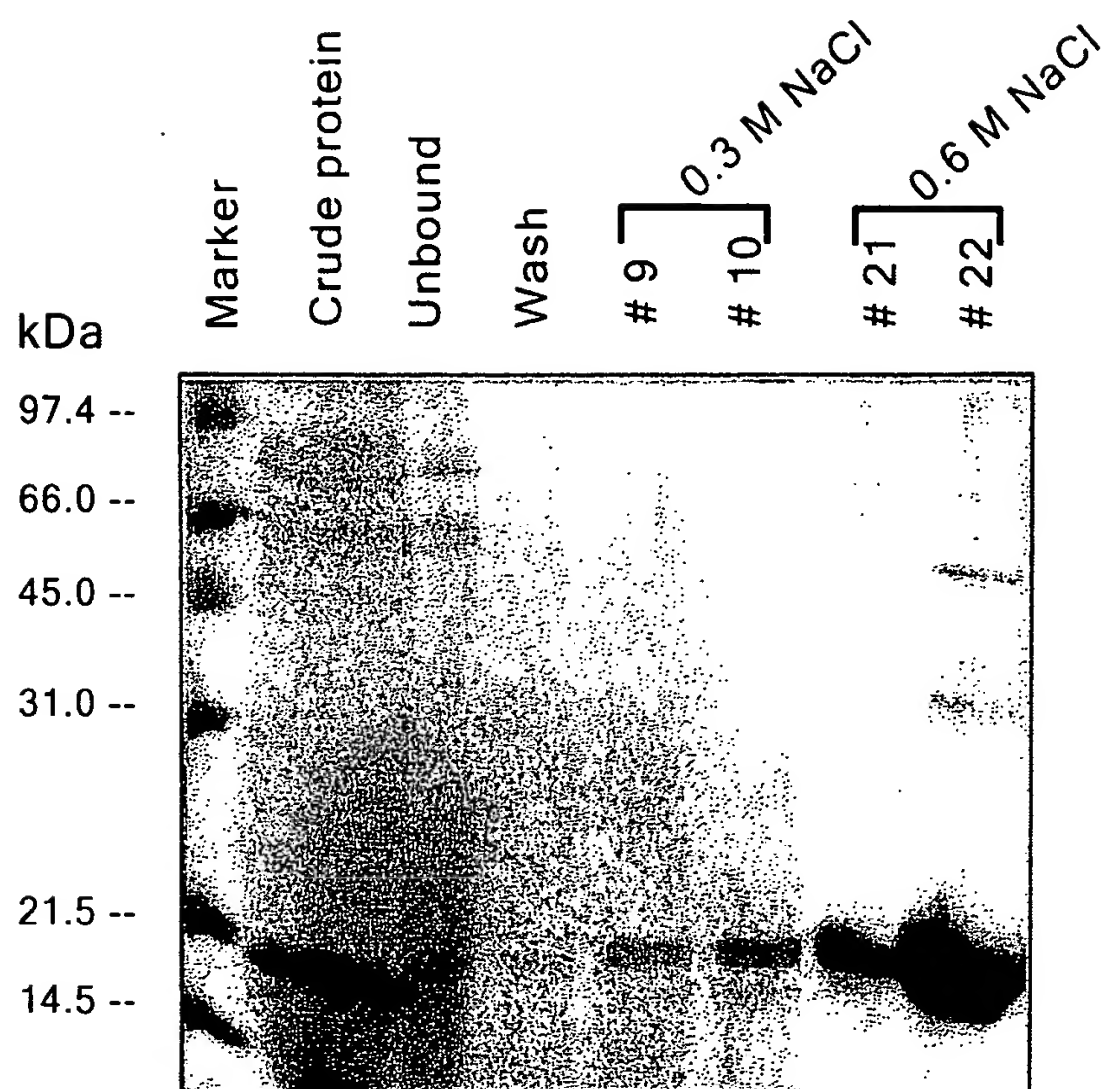


Fig. 6

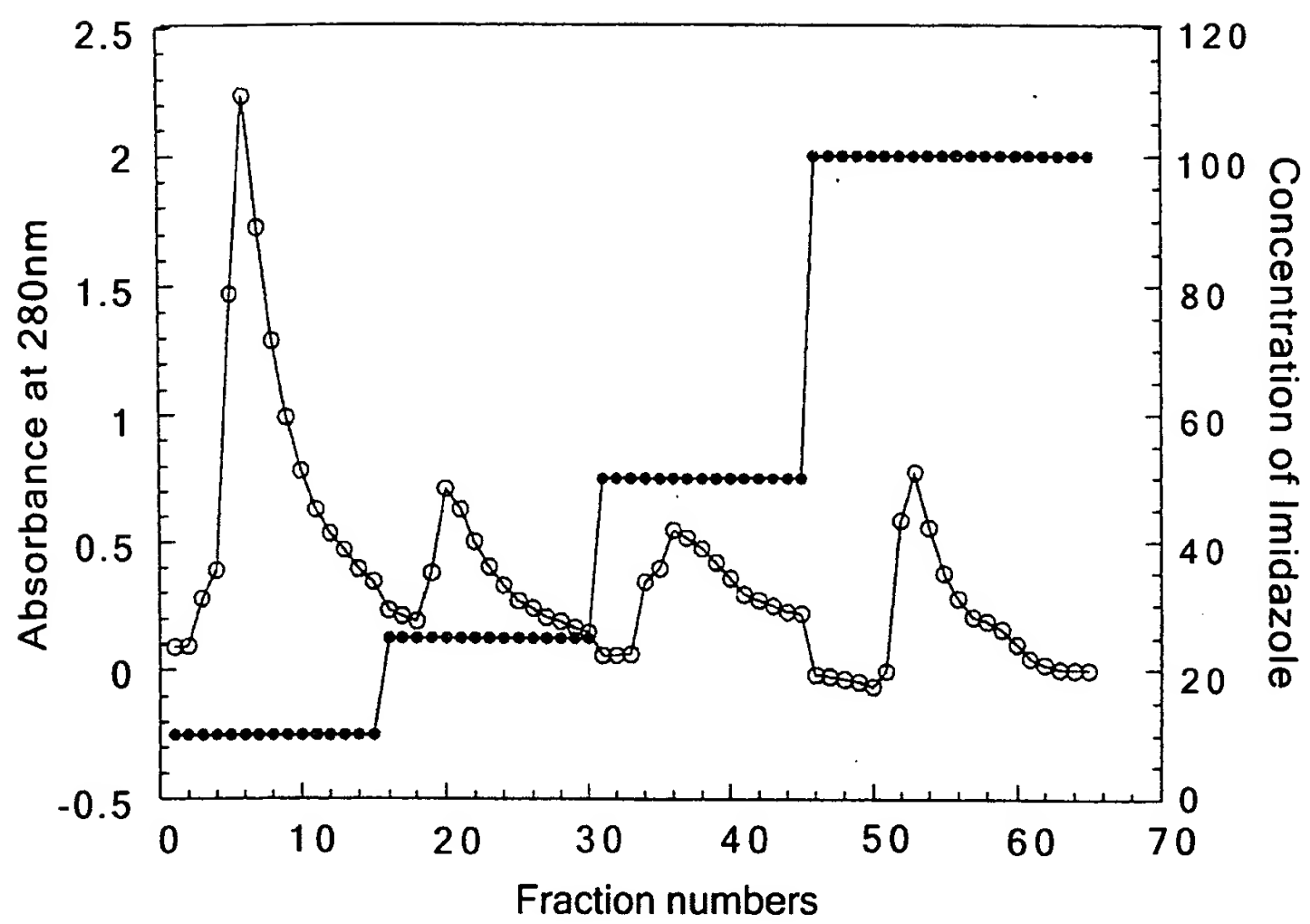


Fig .7

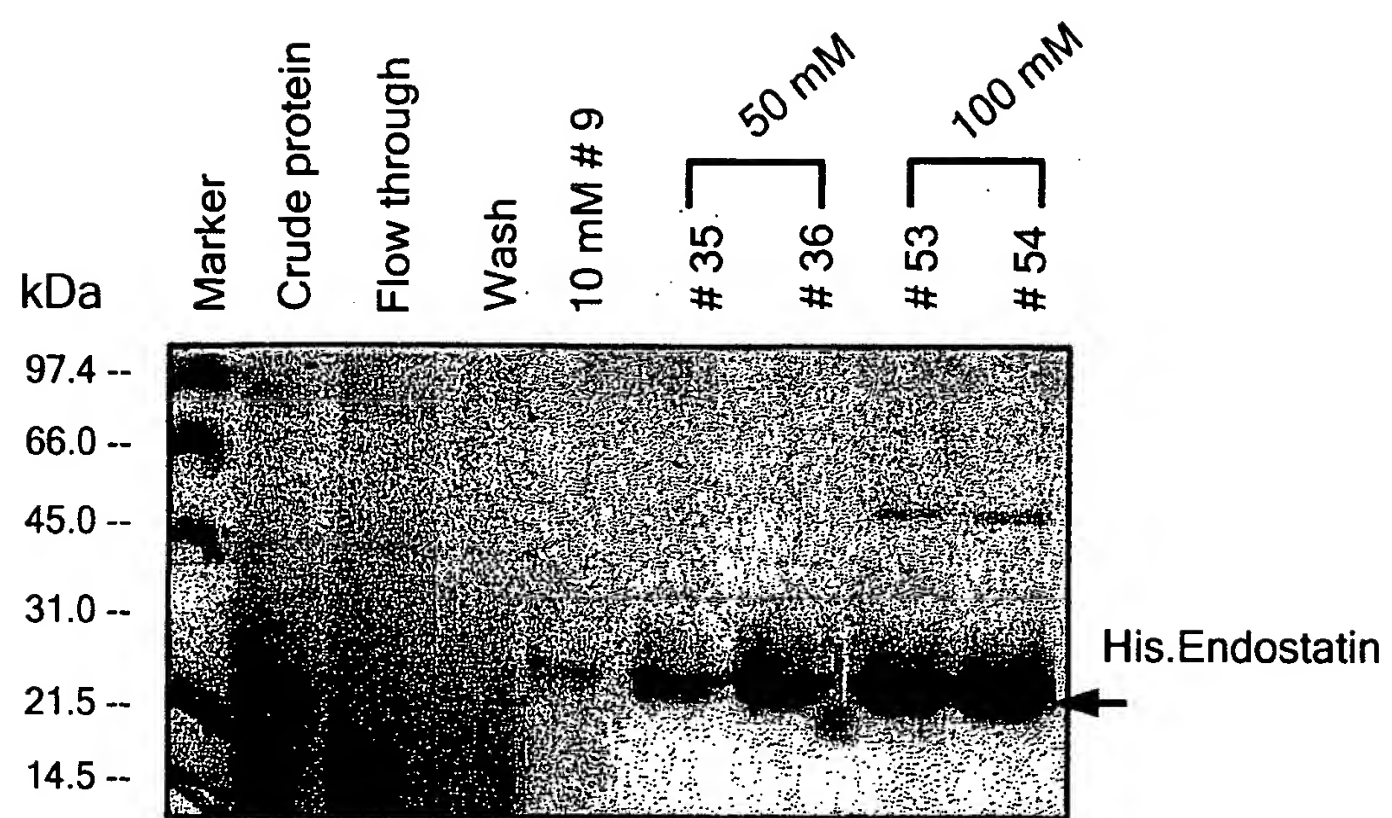


Fig. 8

His.endostatin (bacteria)
Endostatin (yeast)
His.endostatin (yeast)

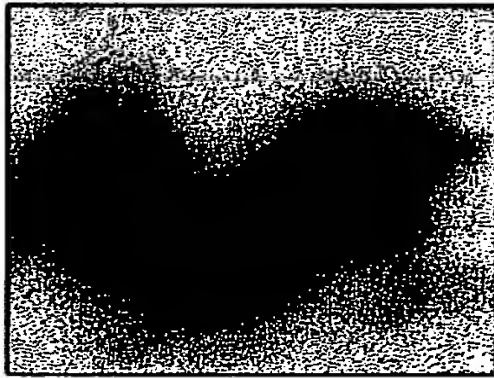


Fig. 9

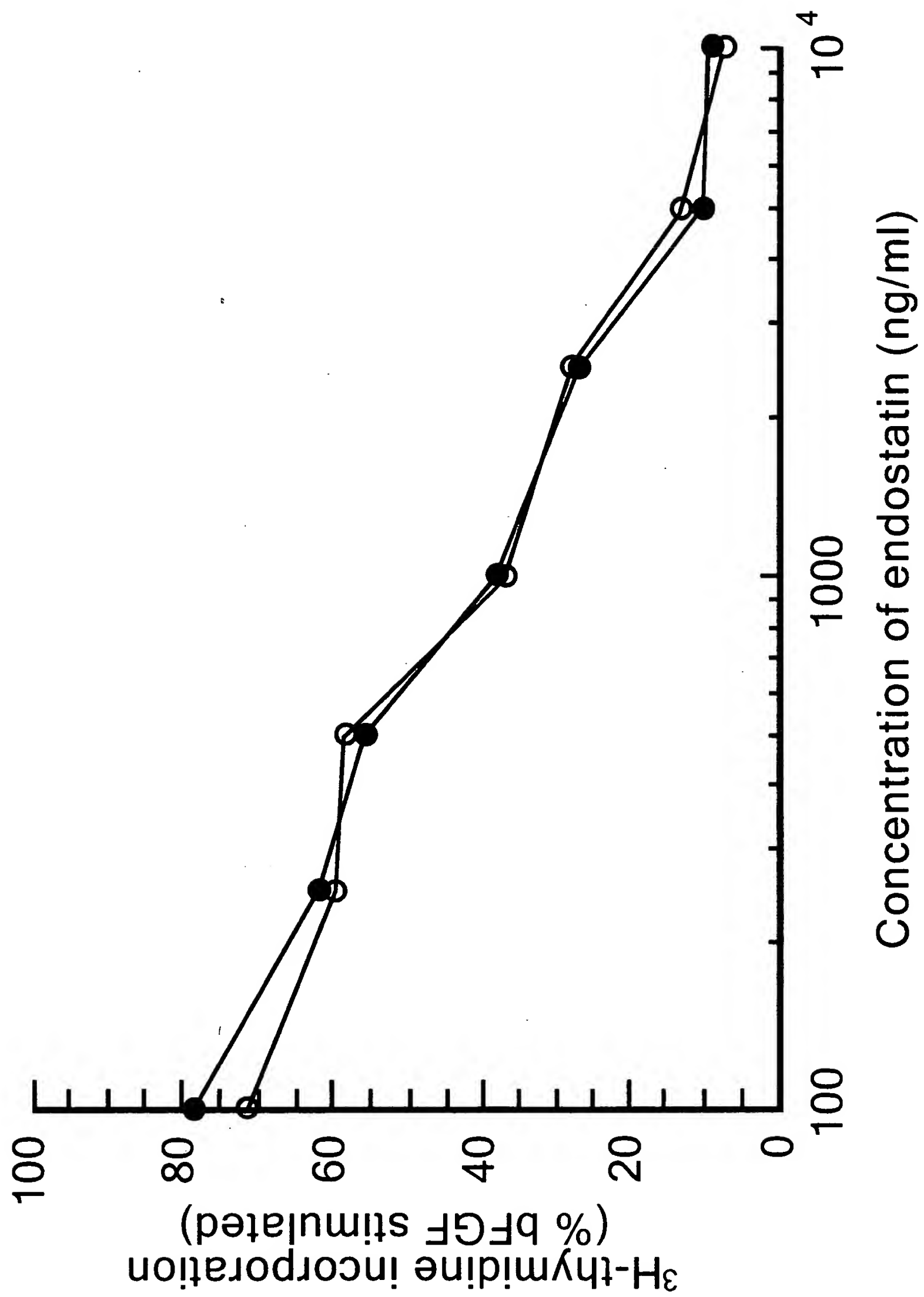


Fig. 10

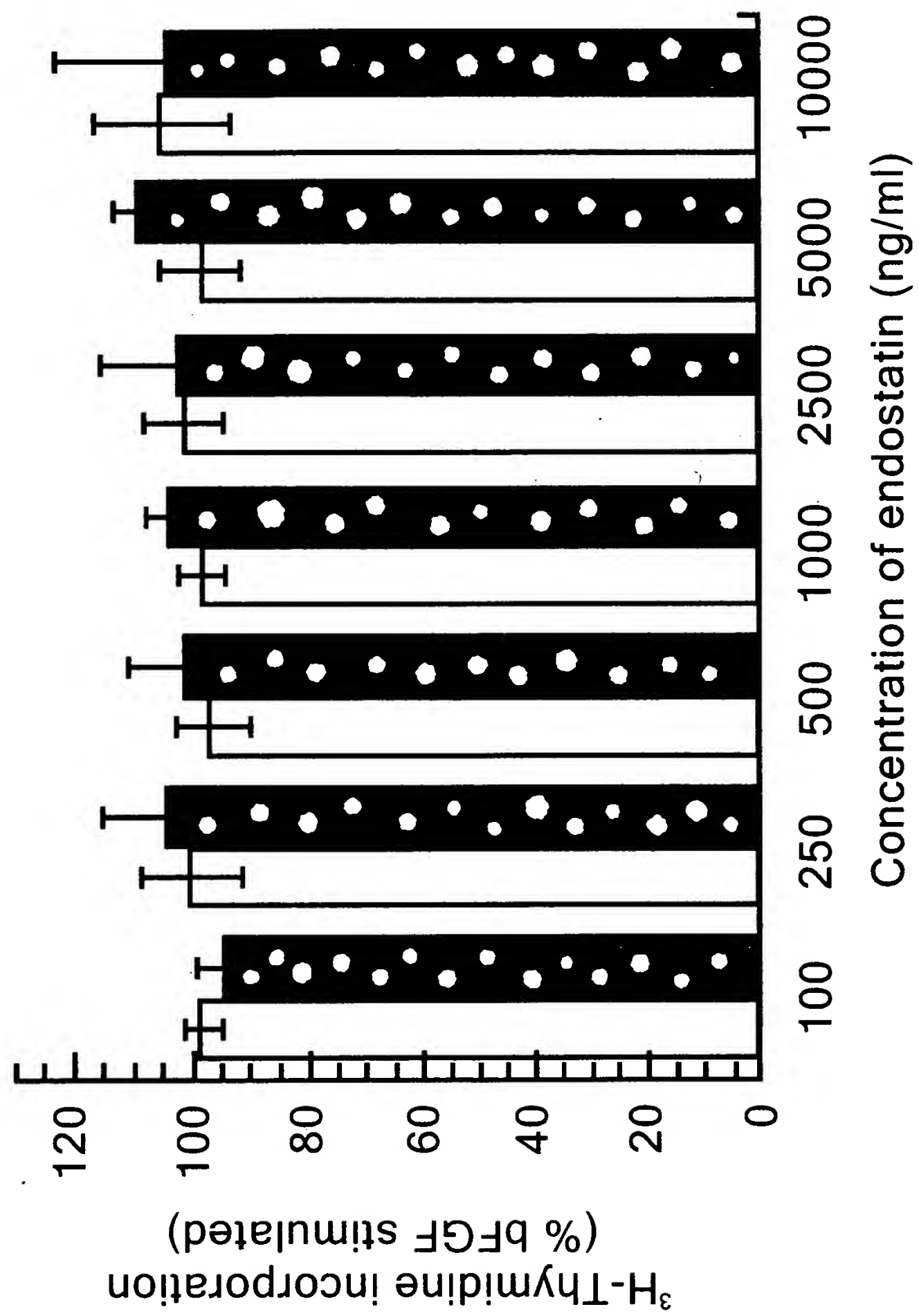
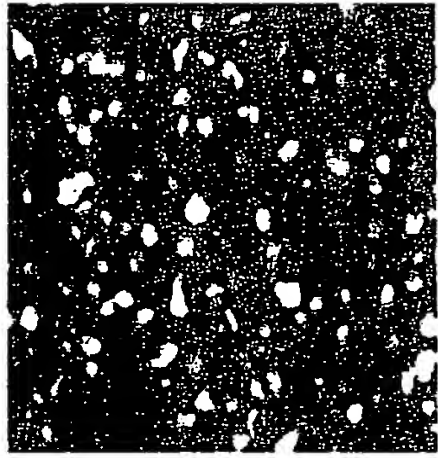


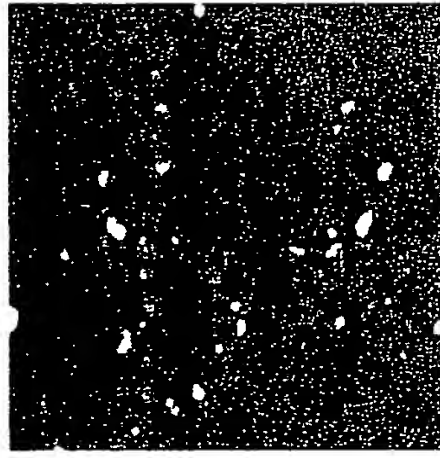
Fig. 11

Fig. 12A



Control +bFGF

Fig. 12B



Endostatin 20 μ g/ml

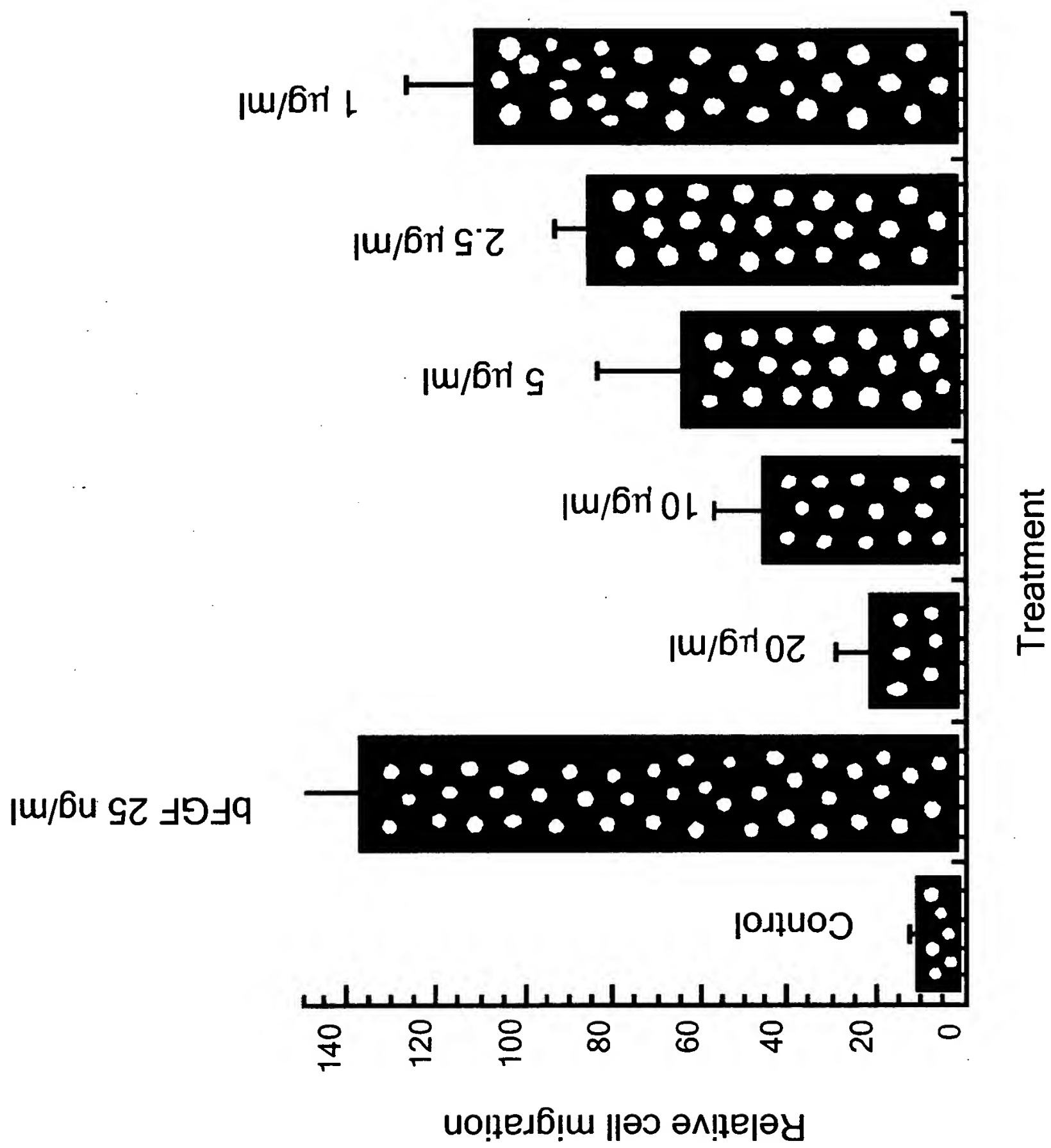
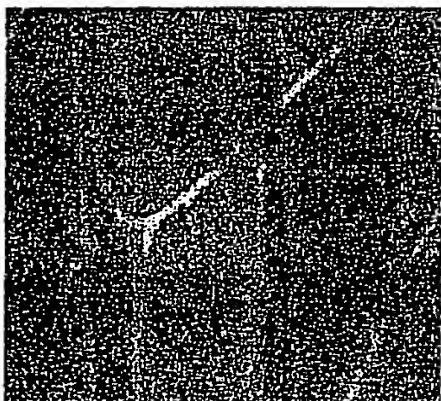


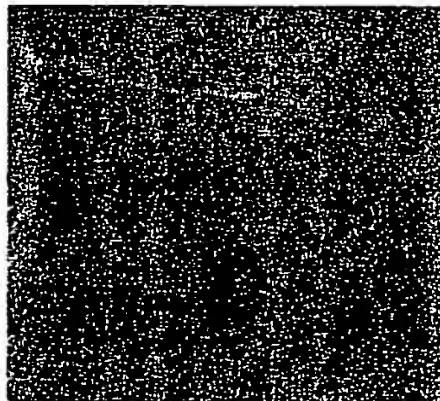
Fig. 13

Fig. 14A



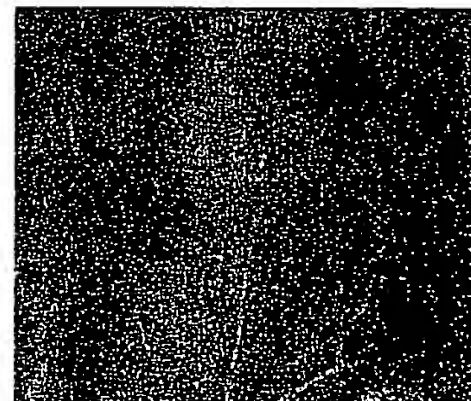
Negative control

Fig. 14B



Positive Control
(VEGF)

Fig. 14C



VEGF +
endostatin 20 μ g

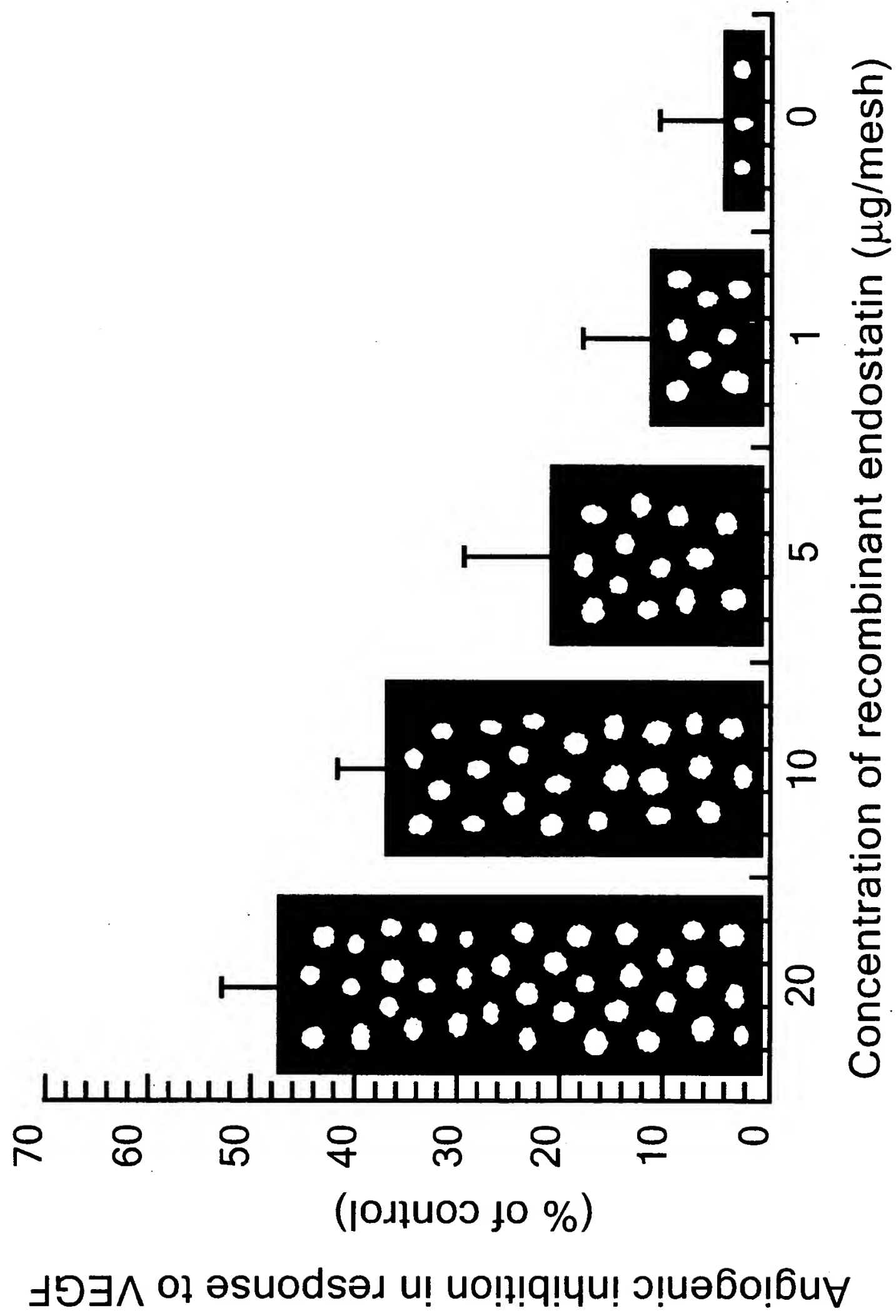


Fig. 15A

Angiogenic inhibition in response to bFGF

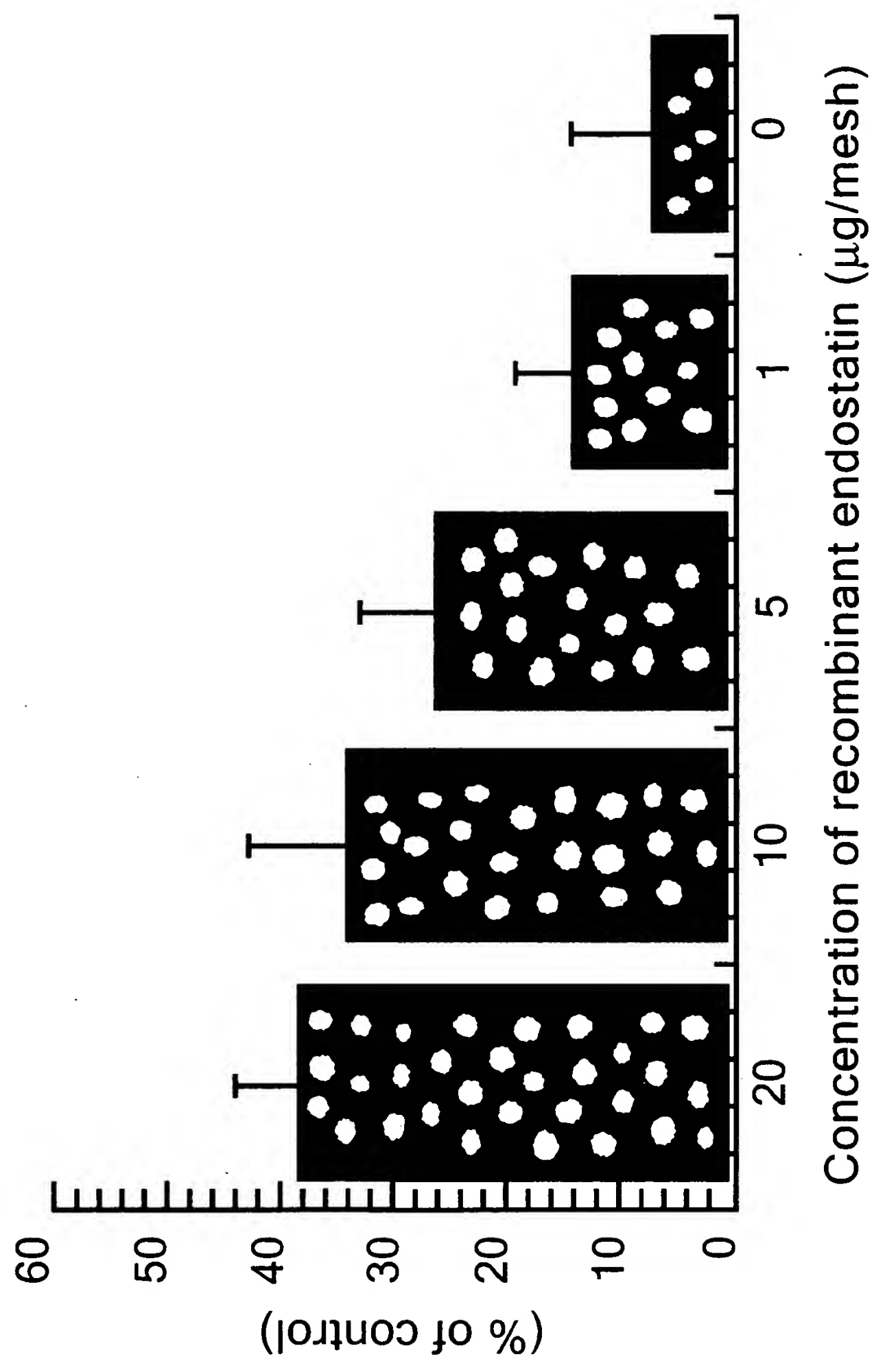


Fig. 15B

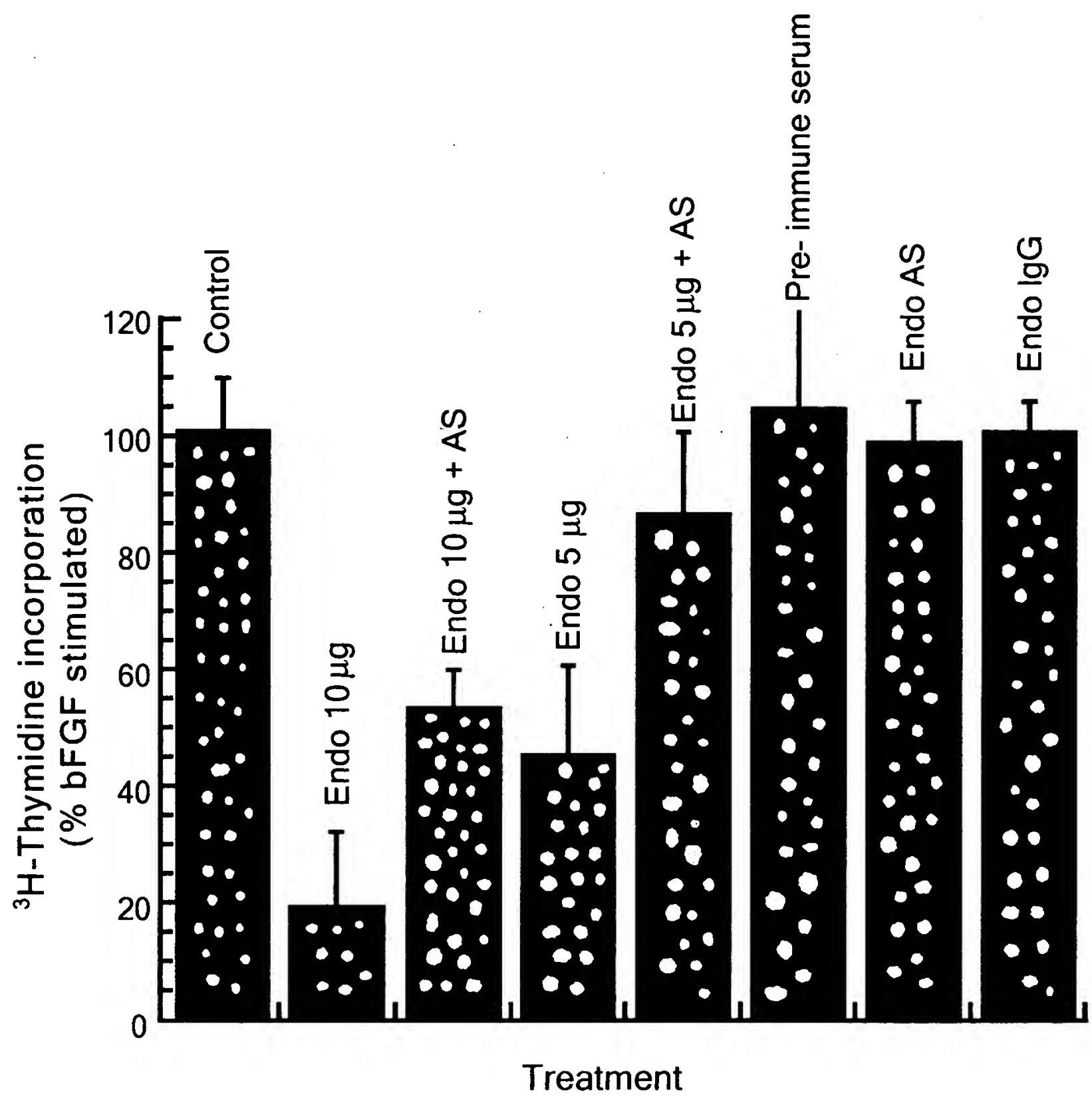


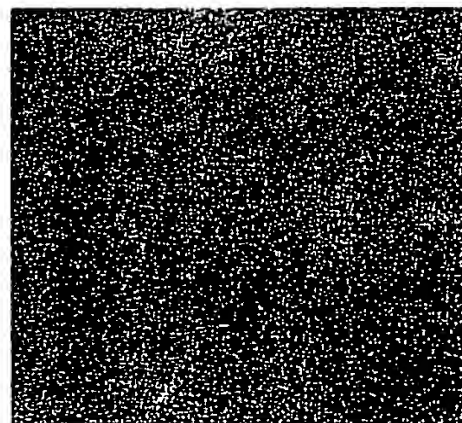
Fig. 16

Fig. 17A



VEGF + endostatin
(10 μ g)

Fig. 17B



VEGF + endostatin (10 μ g) +
polyclonal antiserum (50 μ g)

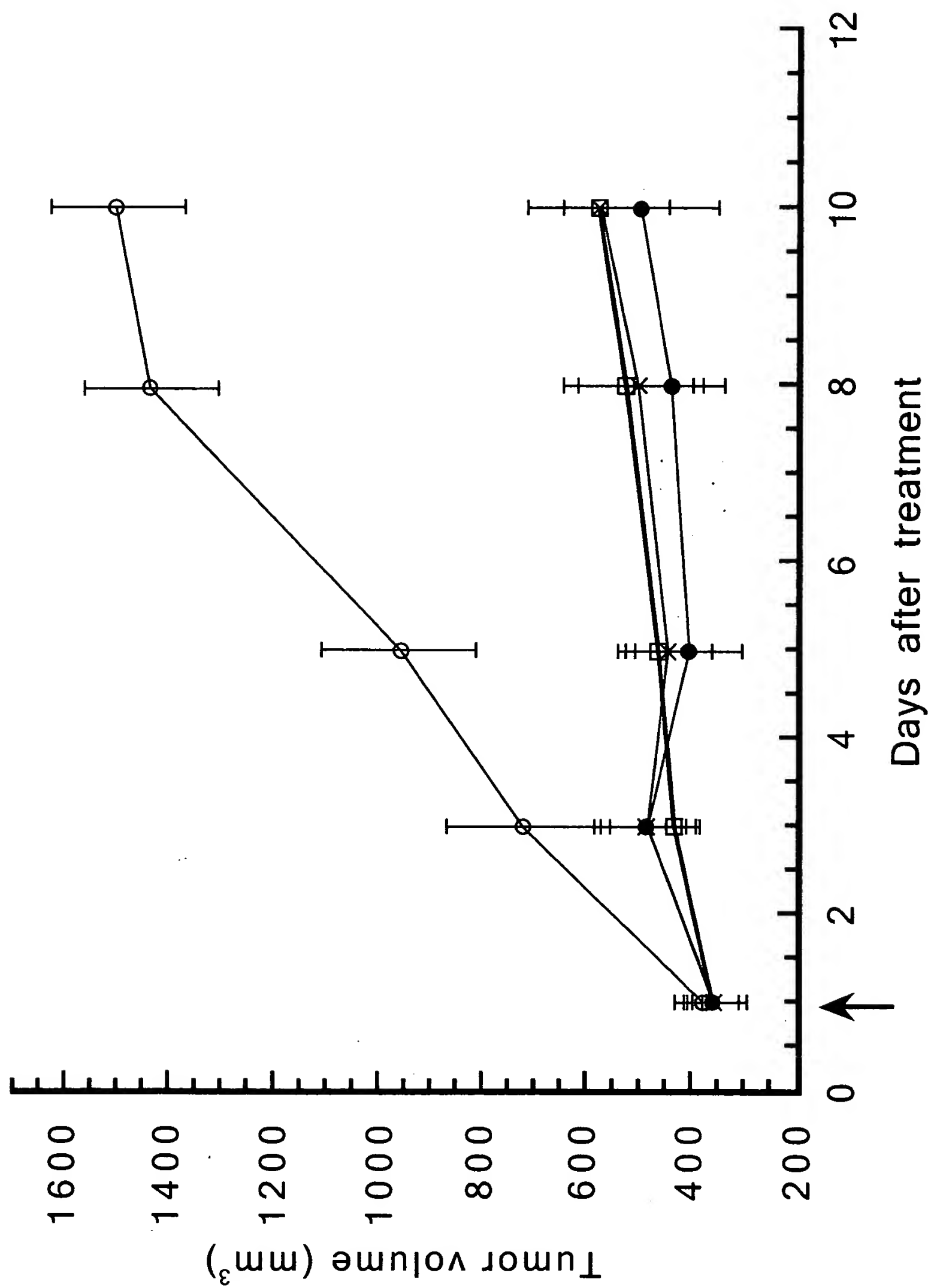


Fig. 18

Fig. 19A

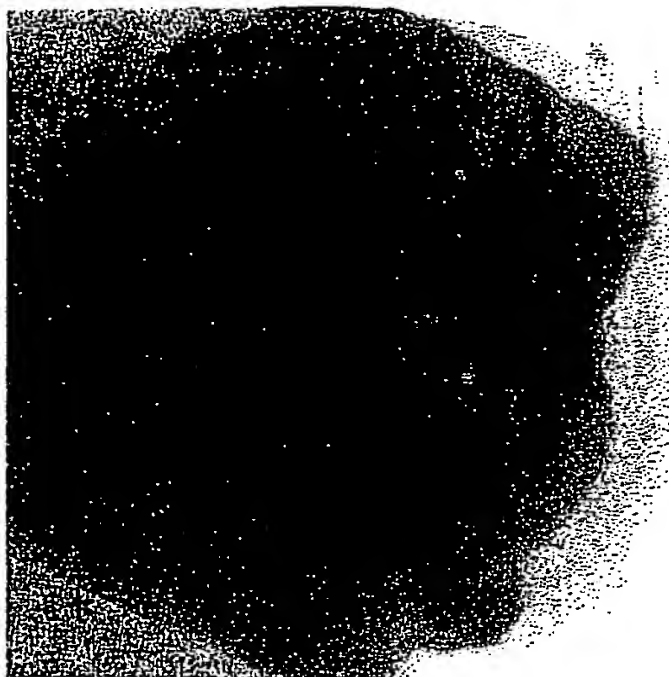


Fig. 19B

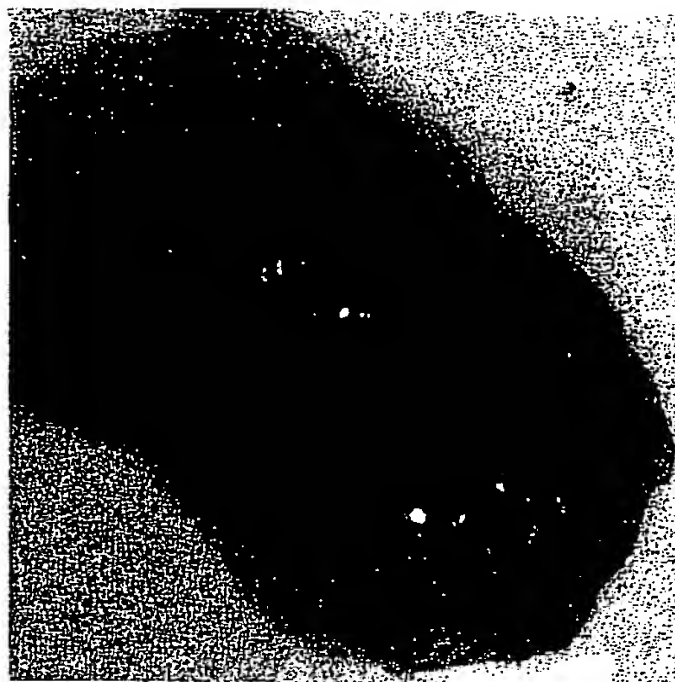


Fig. 19C

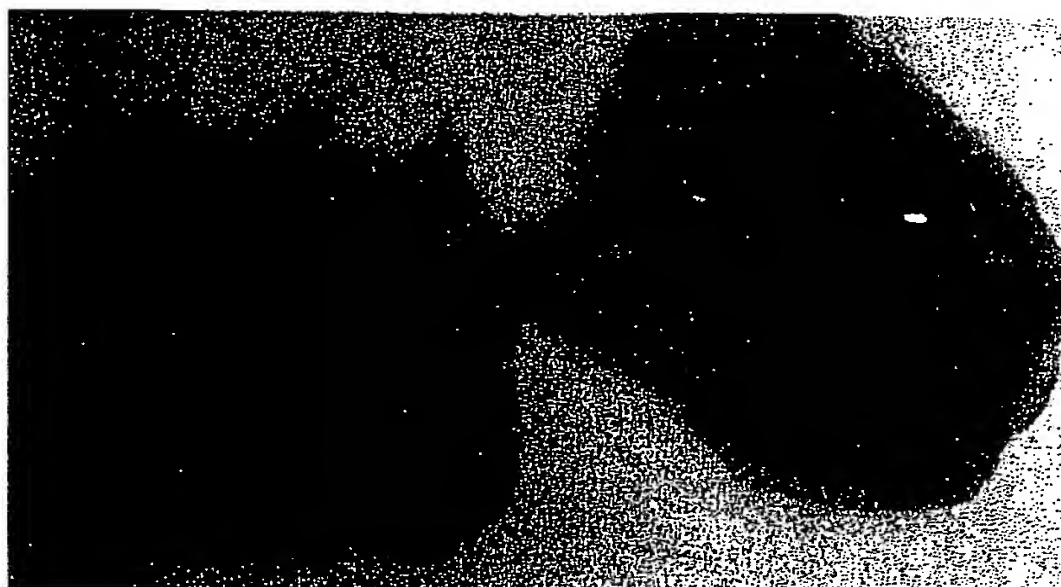


Fig. 19D

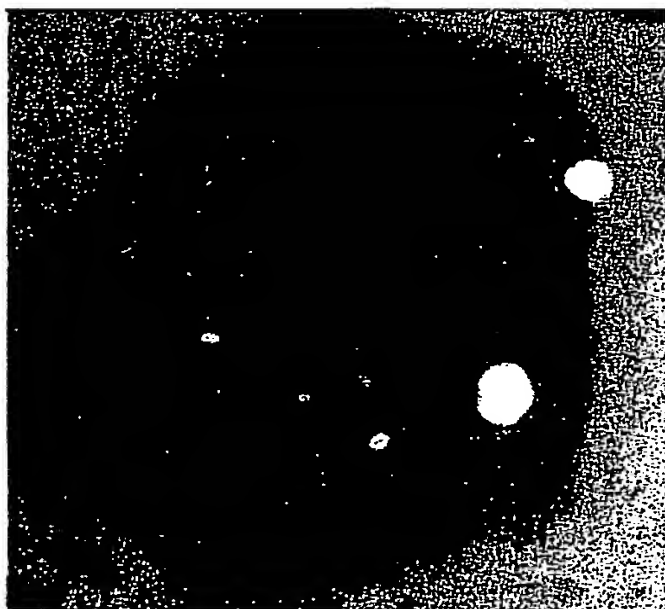


Fig. 19E



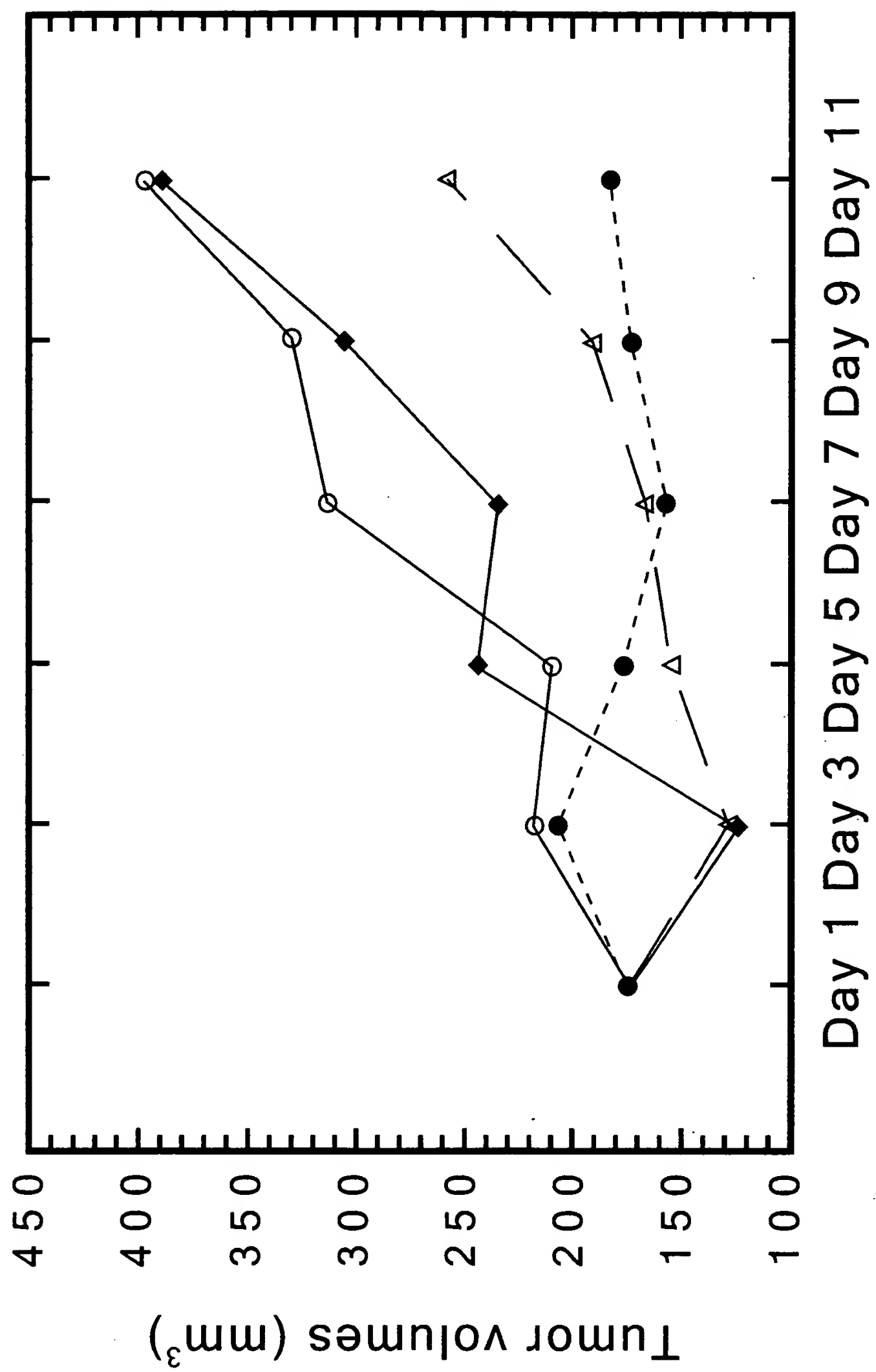


Fig. 20

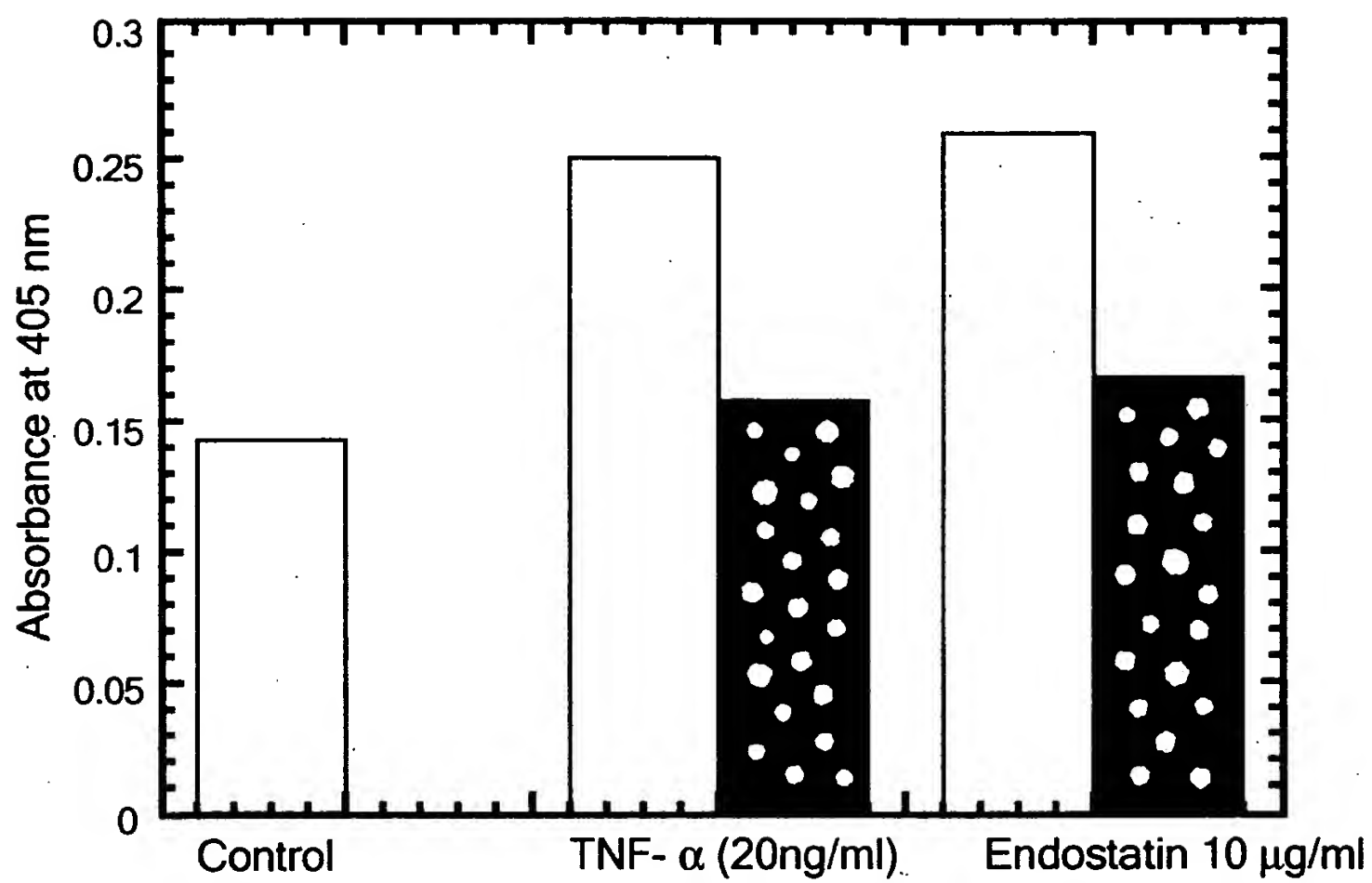


Fig. 21

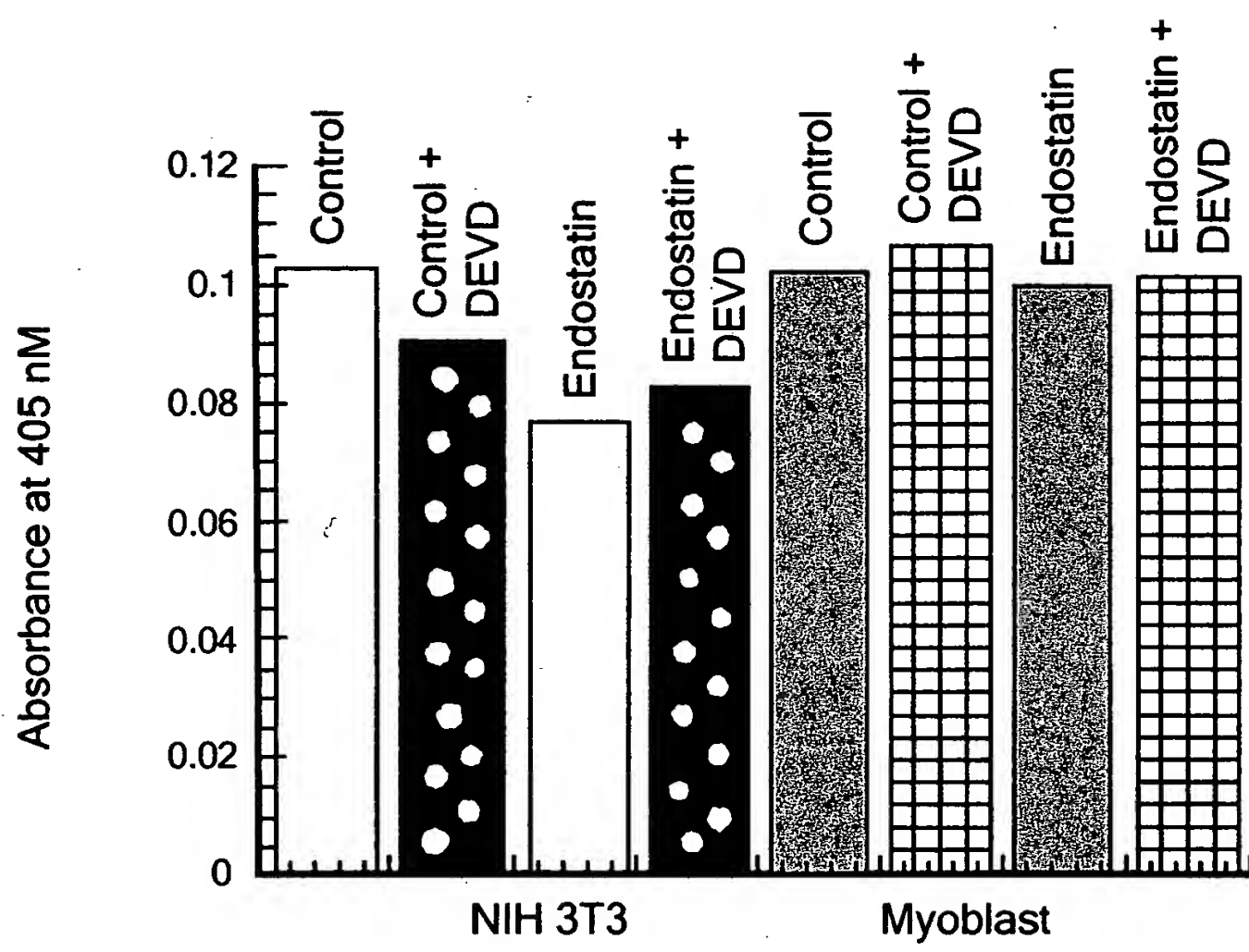


Fig. 22

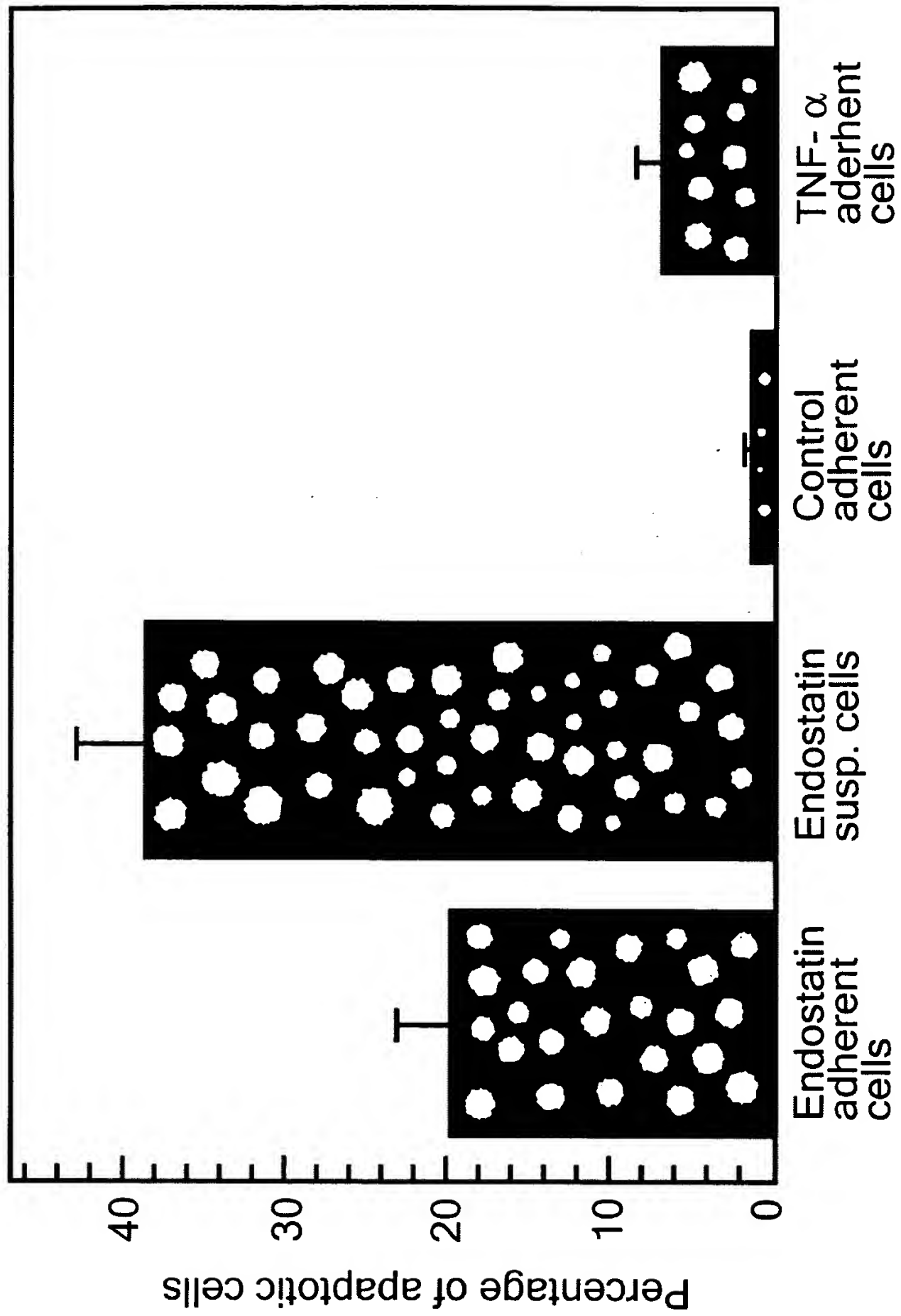


Fig. 23

Fig. 24A

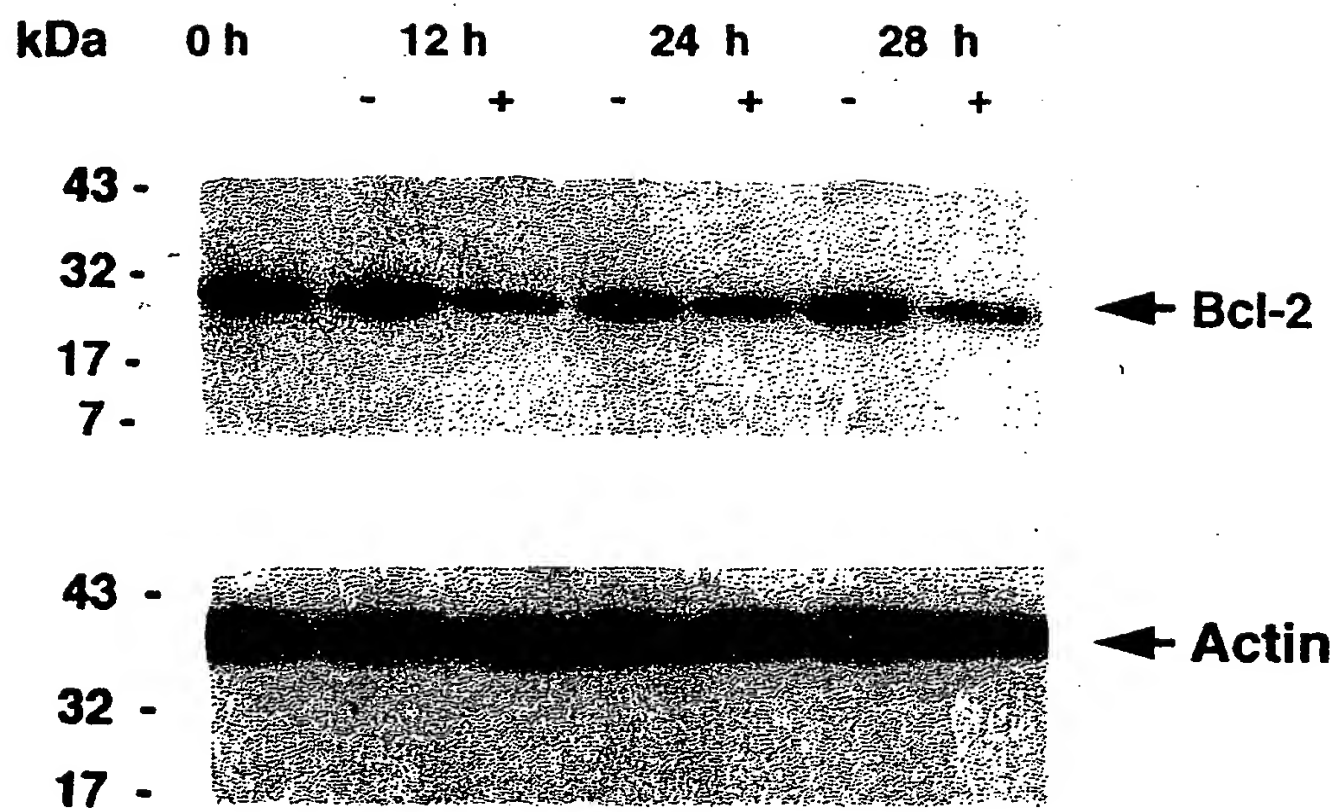
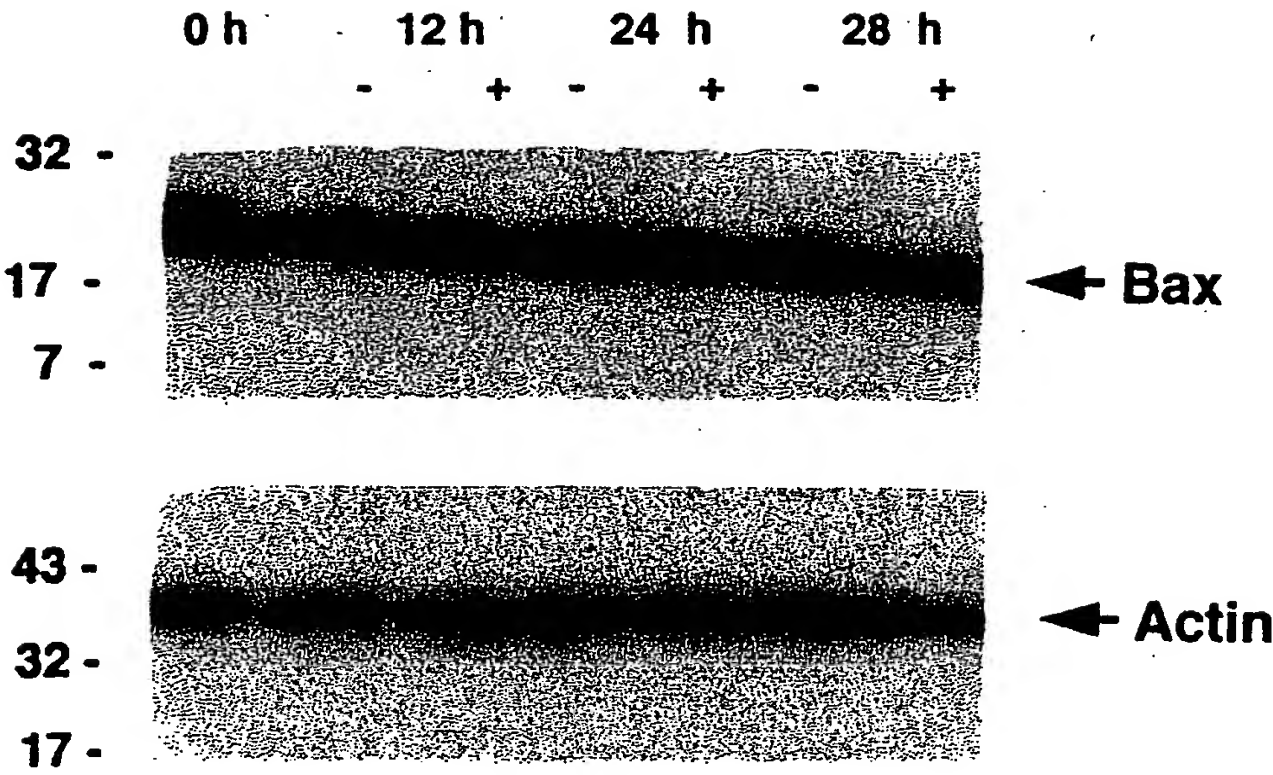


Fig. 24B



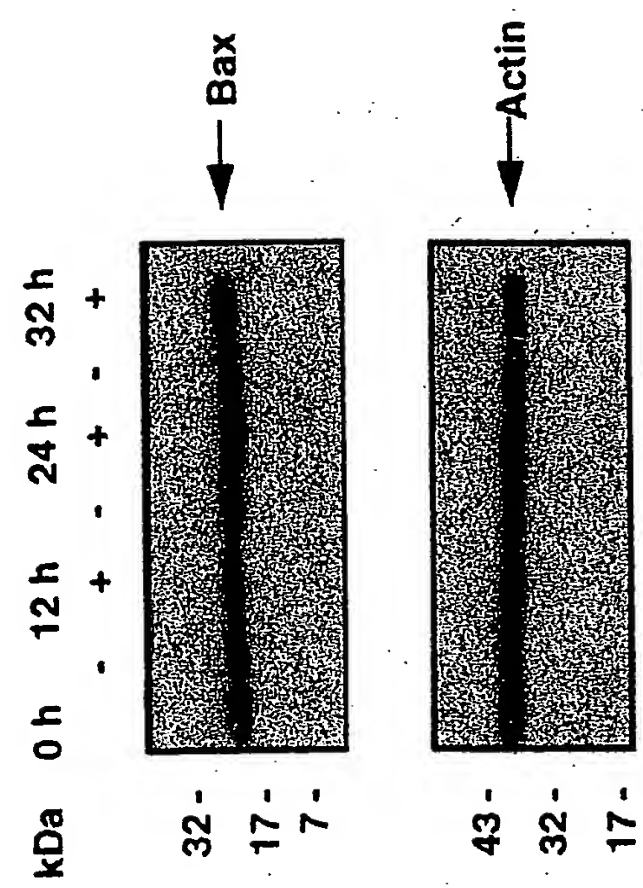


Fig. 25A

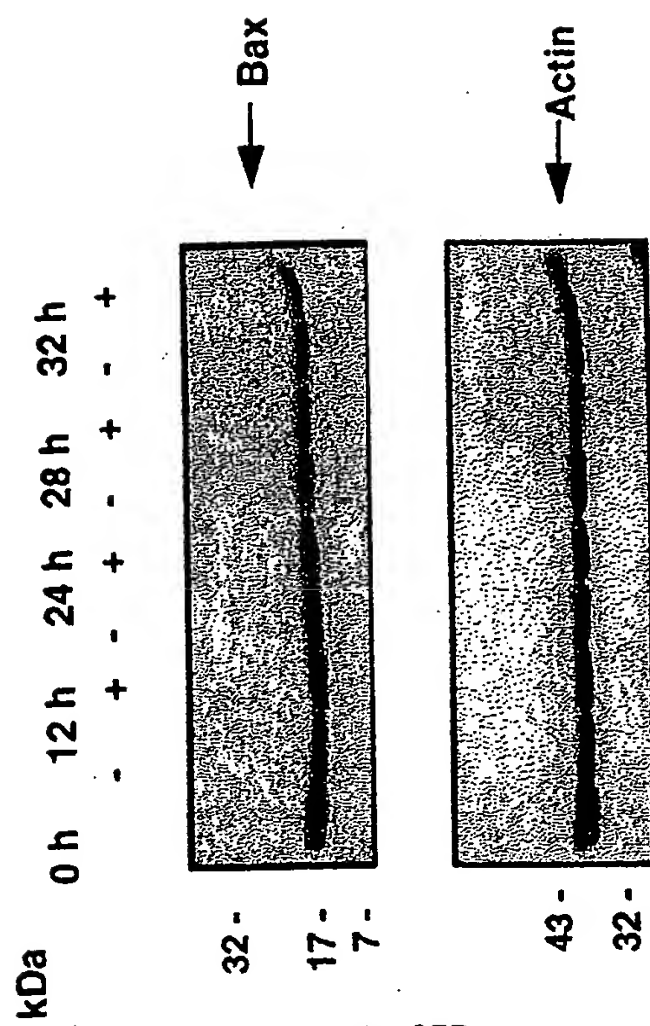


Fig. 25B

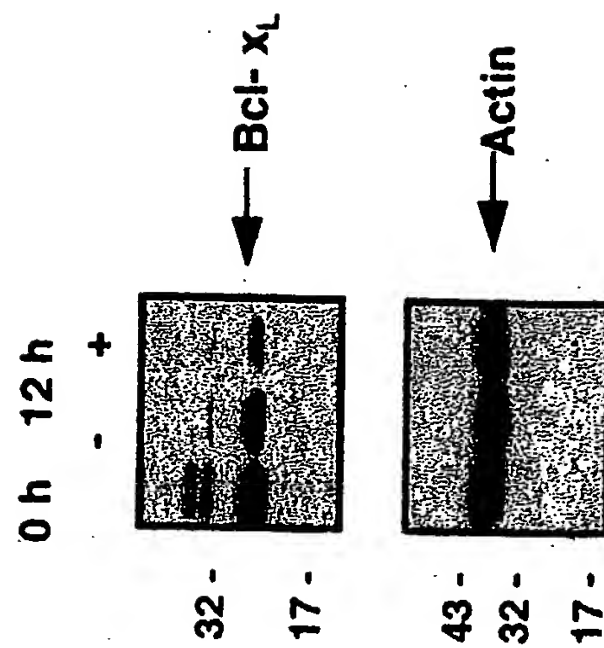


Fig. 25C

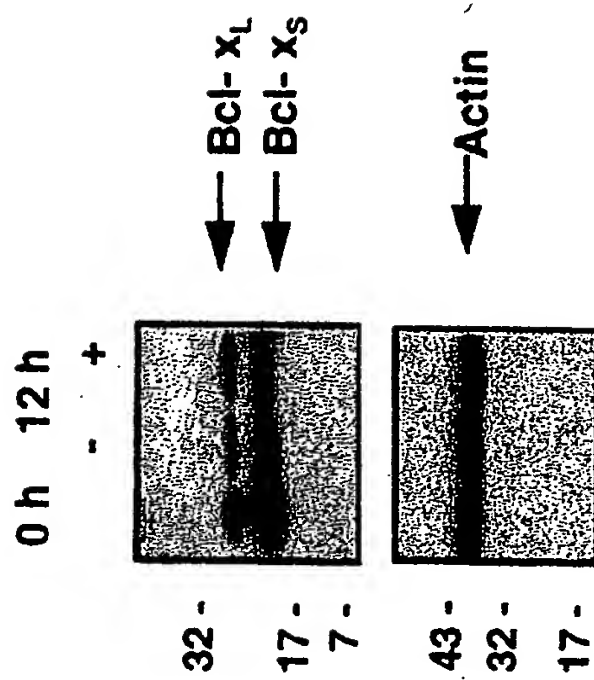


Fig. 25D

Construct Name	Primer Sequence	Cloning Sites	Vector	Protein Sequence
pET17b/ his.mendo	5'-GGC ATA TGC ATA CTC ATC AGG- ACT TT-3' (up) (SEQ ID NO:3)	<i>Nde</i> I & <i>Xho</i> I	Prokaryotic expression, pET	MGHHHHHHHHSSGHIDDDDKH M-mendo (SEQ ID NO:5)
	5' AAC TCG AGC TAT TTG GAG AAA- GAG GT-3' (DOWN) (SEQ ID NO:4)			
pET28a/ mendo	5'-GGC ATA TGC ATA CTC ATC AGG- ACT TT-3' (up) (SEQ ID NO:3)	<i>Nde</i> I & <i>Not</i> I	Prokaryotic expression, pET	MGSSHHHHHHSSGLVPRGSHM- mendo (SEQ ID NO:7)
	5'-AAG CCG CCG CCT ATT TG AGA- AAG AGG T-3' (down) (SEQ ID NO:6)			
pET28a/ EM-1	5' TTC CAT ATG CAT ACT CAT CAG- GAC TTT CAG CCA-3' (up) (SEQ ID NO:8)		Prokaryotic expression, pET	MGSSHHHHHHSSGLVPRGSHM-me ndo (SEQ ID NO:7)
	5' TTA GCG GCC GCC TAC TCA ATG- CAC AGG ACG ATG TA-3' (down) (SEQ ID NO:9)			
pET28a/ EM-2	5' TTC CAT ATG CAT ACT CAT CAG- GAC TTT CAG CCA-3' (up) (SEQ ID NO:8)		Prokaryotic expression, pET	MGSSHHHHHHSSGLVPRGSHM-me ndo (SEQ ID NO:7)
	5' TTA GCG GCC GCC TAG TTG TGG- CAG CTC GCA GCT TTC TG-3' (down) (SEQ ID NO:10)			

Fig. 26A

Construct Name	Primer Sequence	Cloning Sites	Vector	Protein Sequence
pPICZαA/ mendo	5' GGG AAT TCC ATA CTC ATC AGG- ACT TT-3' (up) (SEQ ID NO:11)	<i>Eco</i> RI & <i>Not</i> I	Prokaryotic expression, yeast/pPICZαA	EF-mendo
	5' AAG CGG CCG CCT ATT TGG AGA- AAG AGG T-3' (down) (SEQ ID NO:6)			
pPICZαA/ His.mendo	5'AAG AAT TCC ATC ATC ATC ATC- ATC ACA GCA GC-3' (up) (SEQ ID NO:12)	<i>Eco</i> RI & <i>Not</i> I	Prokaryotic expression, yeast/pPICZαA	EFMGHHHHHHHHSSGHDDDDK HM-mendo (SEQ ID NO:13)
	5' AAG CGG CCG CCT ATT TGG AGA- AAG AGG T-3' (down) (SEQ ID NO:6)			
pPICZαA/ Hendo	5' TTT GAA TTC GCC CAC AGC CAC- CGC GAC TTC CAG CCG GTG CTC- CA-3' (up) (SEQ ID NO:14)	<i>Eco</i> RI & <i>Not</i> I	Prokaryotic expression, yeast/pPICZαA	EF-hendo
	5' AAA AGC GGC CGC CTA CTT GGA- GGC AGT CAT GAA GCT GTT CTC- AA-3' (down) (SEQ ID NO:15)			
pPICZαA/ Restin	5' TTT TTT GAA TTC ATT TCA AGT- GCC AAT TAT GAG AAG CCT GCT CTG CAT TTG-3' (up) (SEQ ID NO:16)	<i>Eco</i> RI & <i>Not</i> I	Prokaryotic expression, yeast/pPICZαA	EF-restin
	5' AAG AAT GCG GCC GCT TAC TTC- CTA GCG TCT GTC ATG AAA CTG- TTT TCG AT-3' (down) (SEQ ID NO:17)			

Fig. 26B

Construct Name	Primer Sequence	Cloning Sites	Vector	Protein Sequence
pPICZαA/ His.Restin	5' AT TCC ATC ACC ATC ACC ATC- ACG- 3' (up) (SEQ ID NO:18)	<i>Eco</i> RI (oligo insertion)	Eukaryotic (Yeast), Pichia, pPICZαA	EFHHHHHHH-restin (SEQ ID NO:20)
	5' AAT TCG TGA TGG TGA TGG TGA- TGG- 3' (down) (SEQ ID NO:19)			
pET28a/ apomigren	5' TTC CAT ATG ATA TAC TCC TTT- GAT GGT CGA GAC ATA ATG AC-3' (up) (SEQ ID NO:21)	<i>Nde</i> I & <i>Not</i> I	Prokaryotic expression, pET	MGSSHHHHHHSSGLVPRGSHM-mendo (SEQ ID NO:7)
	5' AAT GCG GCC GCT TAC TTC CTA- GCG TCT GTC ATG AAA CTG TTT- TCG AT-3' (down) (SEQ D NO:22)			
pET28a/ apomigren	5' AAG AAT TCC ATC ATC ATC ATC-ATC ACA GCA GC-3' (up) (SEQ ID NO:12)	<i>Eco</i> RI & <i>Not</i> I	Eukaryotic (Yeast), Pichia, pPICZαA	EFMGSSHHHHHHSSGLVPRGSHM-apomigren (SEQ ID NO:23)
	5' AAT GCG GCC GCT TAC TTC CTA- GCG TCT GTC ATG AAA CTG TTT- TCG AT-3' (down) (SEQ D NO:22)			

Fig. 26C

**This Page is Inserted by IFW Indexing and Scanning
Operations and is not part of the Official Record**

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images include but are not limited to the items checked:

☐ BLACK BORDERS

☐ IMAGE CUT OFF AT TOP, BOTTOM OR SIDES

☒ FADED TEXT OR DRAWING

☒ BLURRED OR ILLEGIBLE TEXT OR DRAWING

☐ SKEWED/SLANTED IMAGES

☒ COLOR OR BLACK AND WHITE PHOTOGRAPHS

☐ GRAY SCALE DOCUMENTS

☐ LINES OR MARKS ON ORIGINAL DOCUMENT

☐ REFERENCE(S) OR EXHIBIT(S) SUBMITTED ARE POOR QUALITY

☐ OTHER: _____

IMAGES ARE BEST AVAILABLE COPY.

As rescanning these documents will not correct the image problems checked, please do not report these problems to the IFW Image Problem Mailbox.